REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Claims 88-101 are canceled by way of the present Amendment, without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application directed to any subject matter deleted by way of this Amendment.

New claims 102-114 are added herein. Basis for the new claims may be found throughout the specification and claims as filed. Thus, no prohibited new matter is added by way of this Amendment.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 88-101 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 88-101 are canceled herein, and claims 102-114 are added. Thus, in the interest of expediting prosecution, Applicants will address the rejections as they apply to the new claims.

Claim 88 stands rejected as purportedly unclear as to what proviso is to be applied when n=0. The Office Action states that there are two provisos when n=0 and the first one precludes R^5 to be CH_2COOH or CH_2COOMe but the second proviso permits such groups for R^5. Claim 88 is canceled herein. With regard to

new claim 102, Applicants note that only one definition of R^5 is provided when n=0. Thus, Applicants submit that this rejection is mooted.

Claim 93 stands rejected as purportedly indefinite for the recitation of the phrase "n is included between 1 and 8". It is purportedly unclear what is intended. Applicants note that claim 93 has been canceled herein. Corresponding new claim 106 does not recite "n is included between 1 and 8". Thus, Applicants submit that this rejection is mooted.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 88-94 and 100-101 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while enabling for n=0, 1, 2, 3, purportedly does not reasonably provide enablement for n=4, 5, 6, 7, 8.

Claims 88-94 and 100-101 have been canceled herein. Applicants note that new claims 102-114 do not recite compounds wherein n=4, 5, 6, 7 or 8. Instead, the new claims recite compounds wherein n=0,1, 2, or 3, which the Office Action considers to be enabled. Thus, Applicants submit that this rejection is mooted.

Rejections under 35 U.S.C. § 102

For proving anticipation, "anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention as arranged in the claims." Jamesbury Corp. v. Litton Industrial Products, Inc. 225 U.S.P.Q. 253, 256 (Fed. Cir.

1985). The cited references do not describe or suggest all of the elements of the new claims 102-114, as submitted herein.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Wuts *et al.* Wuts *et al.* purported disclose several tetrahydropyran carboxylic acids and esters generically embraced by the instant claims.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Leroux *et al.* Leroux *et al.* purportedly disclose several tetrahydropyran carboxylic acids and tetrahydrofuran carboxylic acids generically embraced by the instant claims.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Newman *et al.* Newman *et al.* purportedly disclose several glycidic esters generically embraced by the instant claims.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Ciurdaru *et al.* Ciurdaru *et al.* purportedly disclose glycidic esters generically embraced by the instant claims.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Reich *et al.* Reich *et al.* purportedly disclose a glycidic ester generically embraced by the instant claims.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Kulesza *et al.* Kulesza *et al.* purportedly disclose several glycidic esters generically embrace by the instant claims.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Genet *et al.* Genet *et al.* purportedly disclose glycidic esters generically embraced by the instant claims.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Chan *et al.* Chan *et al.* purportedly disclose glycidic esters generically embraced by the instant claims.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Bateson *et al.* Bateson *et al.* purportedly disclose tetrahydrofuran carboxylic acids generically embraced by the instant claims.

Applicants submit that Wuts *et al.*, Leroux *et al.*, Newman *et al.*, Ciurdaru *et al.*, Reich *et al.*, Kulesza *et al.*, Genet *et al.*, Chan *et al.*, and Bateson *et al.* all fail to disclose the specific compounds of the claimed invention.

As stated in M.P.E.P. § 2131.02, when the compound is not specifically named in the cited reference, but instead it is necessary to select portions of teachings within a reference and combine them, *e.g.*, select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). One of ordinary skill in the art must be able to "at once envisage" the specific compound within the generic chemical formula, in order for the compound to be anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the

compounds included in the generic formula before any of the compounds can be "at once envisaged." *Id.* Applicants submit that the cited references do not anticipate the presently claimed invention, as the references do not recite the specifically claimed compounds and the skilled artisan would not envisage the particular claimed compounds from the genuses of the cited references.

Thus, Applicants respectfully request that the rejections under 35 U.S.C. § 102 be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 88-89, 95-98 and 100-101 stand rejected under 35 U.S.C. § 103 as purportedly unpatentable over Wang *et al.* ("Wang I") and Huang *et al.* in view of Wang *et al.* ("Wang II").

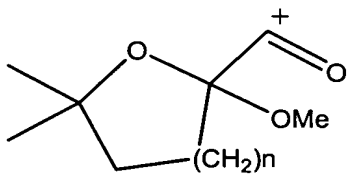
Wang I purportedly disclose the tetrahydrofuran and tetrahydropyran esters of cephalotaxine. The Office Action states that these compounds are known to exhibit antitumor activity. Wang I purportedly differs in not making the tetrahydrofuran or pyran carboxylic acid first. Huang *et al.* purportedly disclose the process for hydrolyzing the cephalotaxine alkaloids and the synthesis of the acid components. Wang II purportedly disclose a process for cyclizing the open chain acid *i.e.,* compound 7 bearing a CTX group to the corresponding tetrahydrofuran compound.

The Office Action states that one having ordinary skill in the art at the time the invention was made would have been motivated to combine both the primary and secondary references and employ the process taught by these prior art to the

starting materials and expect to obtain the desired product because the skilled artisan would have expected the analogous starting materials and reactants to react similarly.

Applicants respectfully traverse.

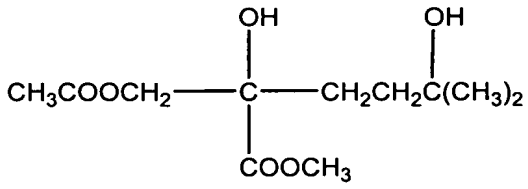
Wang I discloses a tetrahydrofuran and tetrahydropyran ester of cephalotaxine. The synthesis and the starting materials used to obtain these esters is disclosed in Wang II. It is respectfully submitted that neither Wang I nor Wang II teach or suggest syntheses using cycloalkane carboxylic acids or cycloalkane esters, as presently claimed. Wang II teaches the synthesis of the tetrahydrofuran and tetrahydropyran esters of cephalotaxine of Wang I by esterification using mixed cyclic acetals, such as the following intermediate:



After esterification using the mixed cyclic acetals, Wang II teaches a subsequent alpha-hydroxyalkylation using methyl bromoacetate and active zinc under conditions of the Reformatsky reaction to provide a linear ester. The linear ester may then be re-cyclized using p-toluene sulphonic acid to provide a tetrahydrofuran and tetrahydropyran ester of cephalotaxine, as disclosed in Wang I (compounds 8 and 9).

Since Wang I and Wang II teach synthesis of cephalotaxine derivatives using mixed cyclic acetals followed by a Reformansky reaction and subsequent cyclization, neither Wang I nor Wang II teach or suggest syntheses using cycloalkane carboxylic acids or cycloalkane esters, as presently claimed. Therefore, neither Wang I nor Wang II teach or suggest the cycloalkane carboxylic acid and ester intermediates as presently claimed.

As part of a structural study of cephalotaxine alkaloids, Huang teaches mild transesterification of the "harringtonines" to yield cephalotaxine and the respective dimethyl esters of hydroxydicarboxylic acids (compounds 7-10). All of these hydroxydicarboxylic acids are linear nor cyclic compounds. For example compound 7 is as follows:



Huang teaches methods to determine which of the carboxyl groups of the dimethyl esters of hydroxydicarboxylic acids was originally esterified in cephalotaxine. Huang relates to determining the gross structures of the harringtonines. Therefore, Huang is concerned with determining the structures of the four closely related dimethyl esters of the harringtonines. As described above, Wang II relates to synthesizing cephalotaxine derivatives.

There is no teaching or suggestion in Wang II or Huang to combine the methods of synthesis and resulting cephalotaxine derivatives of Wang II with the methods to determine which of the carboxyl groups of the dimethyl esters of hydroxydicarboxylic acids was originally esterified in cephalotaxine of Huang. Neither Wang II nor Huang teach or suggest the cycloalkane carboxylic acid and ester intermediates as presently claimed.

Claims 88-89 and 100 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Tsujihara *et al.* Tsujihara *et al.* purportedly disclose several epoxypropionic acids useful as intermediates to make baccatin derivatives, which includes compounds claimed herein. Tsujihara *et al.* purportedly disclose both the equivalency of herein exemplified substituted phenyl with those substituents claims for X claimed herein. The Office Action states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to make compounds variously substituted epoxypropionic acid as permitted by the reference and expect resulting compounds to possess the uses disclosed by the art in view of the equivalency teaching outlined above. Applicants traverse.

Applicants submit that the claimed invention is not obvious over Tsujihara *et al.*, as the references does not recite or even suggest the specifically claimed compounds. Thus, the skilled artisan would not arrive at the specifically claimed compounds of the present invention from the disclosure of Tsujihara *et al.*

Applicants respectfully request that the rejections under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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